REMARKS

All pending claims (43-45, 49, 56-59 and 61-64) have been cancelled and new claims 65-76 submitted. Applicants actions do not signal agreement with the Examiners comments or position; the previous claims were canceled and new claims submitted for clarity and the convenience of the Examiner and the Applicants. The newly submitted claims substantially track the previous claims.

New claim 65 tracks previous claims 43 and 61; however, the language has been amended so the claimed protein comprises an at least 6 amino acid portion from SEQ ID NO:62. Support for such portions can be found in the specification, for example, on page 13, lines 21-25, through page 14, lines 1-2, and on page 17, lines 11-18. In addition, claims 65 and 73 now specify the function of eliciting an immune response. Claims 66, 67, 74 and 75 specify particular types of immune responses. Support for these functions can be found in the specification, for example, on page 14, lines 15-21, page 41, lines 3-23, through page 52, lines 1-21.

Claim 68 specifies the claimed protein comprise an at least 38 amino acid portion from SEQ ID NO:62. Support for 38 amino acid fragments can be found in US Patent 5,795,862 to which the instant Application traces its priority. US Patent 5,795,862 discloses SEQ ID NO:6 which represents the N-terminal 38 amino acids from PfspI.

Claims 69 and 70 track previous claims 49 and 59, respectively.

Claims 71 and 76 track previous claims 63 and 64, respectively. Claim 72 substantially tracks previous claim 64; however, the claimed fragment is specified as being at least 6 contiguous amino acids of SEQ ID NO:62. Support for such fragments can be found in the specification, for example, on page 13, lines 21-25, through page 14, lines 1-2, and on page 17, lines 11-18.

Priority Claim

Applicants note the specification has been amended to correct the priority claim. Specifically, the instant Application now properly references the complete chain of priority from U.S. Patent Application 09/171,156, which should also include U.S. Patent No. 5,795,862 and U.S. Patent No. 5,646,115 as set forth in the amendment above, which patents disclose SEQ ID NO:6, a 38 amino acid fragment from PfspI.

Specification/Informalities

Previously the Examiner stated the title of the invention was not descriptive. Applicants have submitted a new title which they believe adequately describes the instant invention.

Claim Objections

The Examiner objected to claim 57 as being grammatically incorrect. Applicants note claim 57 has been canceled; the language of claim 57 is not present in the newly submitted claims.

The Examiner objected to claim 61 stating it was a substantial duplicate of claim 43. Applicants note both claim 61 and 43 have been canceled.

Rejections Under 35 USC §112, First Paragraph- Written Description

The Examiner has rejected Claims 43-45, 49, 56-59 , 61-62 and 64 as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. Specifically, the Examiner states the specification lacks support for the limitation "at least 38 amino acids". Applicants note that while this limitation has been removed from the main claim, it is now present in newly submitted claim 68. Therefore, Applicants will address this rejection below.

Applicants had previously argued support for this limitation could be found in US Patent 5,795,862 to which the instant application claims priority. The Examiner correctly noted Applicants previously failed to properly claim priority to US Patent 5,795,862. Applicants have now corrected this defect (see "Amendments to the Specification" above); the instant Application now properly claims priority to US Patent 5,795,862 which discloses SEQ ID NO:6, a 38 amino acid fragment from PfspI (SEQ ID NO:62). Since SEQ ID NO:6 clearly represents a 38 amino acid fragment of SEQ ID NO:62, Applicants submit the disclosure of SEQ ID NO:6 provides support for fragments of at least 38 amino acids from SEQ ID NO:62.

The Examiner previously stated that even if the instant Application properly claimed priority to US Patent 5,795,862, the disclosure of SEQ ID NO:6 fails to provide support for the limitation of "at least 38 amino acids" since the 38 contiguous amino acids recited in the claims is not limited to the 38 amino acids of SEQ ID NO:6 but instead encompass any 38 contiguous amino acids of

SEQ ID NO:62. Applicants respectfully disagree with the Examiners conclusion. It is clear from the specification that the inventors contemplated the use of full-length flea saliva proteins as well as fragments or portions of such proteins (although the specification refers to any flea saliva protein, future discussion will be limited to PfspI which is the subject of the instant claim set). In support of this, the Examiner's attention is directed to the specification, for example, page 12, lines 24-25, through page 13, lines 1-2, page 15, lines 6-22, and page 17, lines 4-26, through page 18, lines 1-4. These sections of the specification clearly state useful PfspI proteins of the instant invention can be full-length proteins or portions thereof including truncation fragments. Further, these sections illustrate that Applicants did not intend to limit the claims to a particular portion of PfspI. Instead, Applicants contemplated the use of any portion that is useful for the detection or treatment of allergic dermatitis; see specifically, for example, page 17, lines 19-26 , which state proteins of the present invention include truncated homologues and proteolytic products and page 14, lines 15-18 which state preferred saliva proteins include at least one epitope capable of eliciting a hypersensitive response to a natural saliva protein counterpart. Applicants contend sections of the specification such as those cited above clearly demonstrate the inventors contemplated the use of any fragment of the full length PfspI protein capable of eliciting an immune response against the full length protein.

With regard to a particular fragment size, Applicants clearly envisioned the use of fragments of at least 6 amino acids of PfspI (see, for example, page 13, lines 21-25, through page 14, lines 1-2.) However, the specification states 6 amino acids is the minimal size, meaning proteins 6 amino acids in length up to the full length (155 amino acids) were contemplated. While the Examiner maintains the specification fails to describe more than one representative from the claimed genus, Applications disagree. The full length sequence of PfspI is clearly disclosed (SEQ DI NO:62). Applicants are claiming 6 amino acid fragments from the full length sequence. While every possible 6 amino acid fragment of SEQ ID NO:62 is not individually listed in the specification, Applicants contend that by disclosing the full length sequence, Applicants have inherently disclosed all possible fragments as well. After all, the full length sequence is nothing more than the collective sum of every possible fragment of the whole. One skilled in the art could easily read the full length sequence and from that

sequence, construct all 149 possible 6 amino acid fragments. Likewise, one skilled in the art could read the full length sequence and construct all 117 possible 38 amino acid fragments.

Applicants recognize that in response to previously presented arguments similar to the ones given above, the Examiner has stated such arguments are not commensurate in scope with the claimed invention since the claimed genus encompasses all species comprising a fragment of SEQ ID NO:62. Applicants have argued sequences outside of the core SEQ ID NO:62 fragment are irrelevant. The Examiner disagreed contending, contrary to Applicants assertion, sequences flanking the core SEQ ID NO:62 fragment are highly relevant. Applicants respectfully disagree with the Examiners contention.

To begin with, the Examiner has argued sequences flanking the core SEQ ID NO:62 fragment are a critical feature of the invention. Applicants disagree. The critical feature of the instant invention is the sequence of PfspI or useful fragments of this sequence. Applicants have disclosed the full length of PfspI (SEQ ID N:62) and inherently, all possible contiguous fragments of this sequence. Furthermore, Applicants note the claims have been amended to include a functional limitation; however, Applicants note the function is tied to the SEQ ID NO:62 sequence fragment, not the entire protein. Claim 65 states the claimed protein must have an at least 6 contiguous amino acid sequence from SEQ ID NO:62, wherein the 6 contiguous amino acid sequence elicits an immune response to the full length PfspI protein; the functional limitation has been limited to the SEQ ID NO:62 fragment. Therefore, because the functional activity is limited to the SEQ ID NO:62 sequence fragment, Applicants contend the sequences flanking this fragment become irrelevant. As long as a protein contains an at least 6 amino acid (or 38 amino acid) sequence from SEQ ID NO:62 and as long as that core sequence, by itself, can elicit an immune response to the full length PfspI, then the protein falls within the scope of the instant claims. Since Applicants have disclosed all possible PfspI fragments and since they have also linked these clearly defined structures to a disclosed function, Applicants believe the instant claims satisfy the written description requirements.

Rejections Under 35 U.S.C. §112, First Paragraph - Enablement

The Examiner has rejected claims 43-45, 57-58 and 61-62 under 35 U.S.C. §112, first paragraph, for lack of enablement. Specifically, the Examiner states undue experimentation would

be required for a skilled artisan to make or use the entire scope of the claimed invention. In reaching this determination, the Examiner cites the following factors:

- the claims are so broad as to encompass all proteins comprising a fragment of SEQ ID NO:62 and having any biological activity. The Examiner states the disclosure is limited to the protein of SEQ ID NO:62.

- the specification provides only a single working example of PfspI, i.e., SEQ ID NO:62, which fails to provide the necessary guidance for making and/or using the entire scope of the claimed proteins. The Examiner states the specification fails to provide guidance regarding amino acids of SEQ ID NO:62 that may be altered by substitution, addition, insertion and/or deletion and fails to provide guidance as to how to use variant proteins having activities other than the desired activity.

- it is highly unpredictable as to which alterations in a proteins amino acid sequence can be made with the expectation of maintaining he ability of an antibody to bind the altered sequence. Further, the state of the art supports a high level of unpredictability.

- undue experimentation would be required to screen all variants of a protein having any function.

Applicants disagree with the Examiner's conclusion that undue experimentation would be required to practice the instant invention. First, Applicants note the claims as currently drafted do not encompass all proteins comprising a fragment of SEQ ID NO:62, having any biological activity. As described above, the claims encompass proteins comprising an at least 6 contiguous amino acid fragment from SEQ ID NO:62 where the SEQ ID NO:62 fragment can elicit an immune response to the full length PfspI protein. While a large number of proteins may comprise a fragment of SEQ ID NO:62, not all of theses fragments will have the prescribed activity. Since it is the SEQ ID NO:62 fragment in which the activity resides, not all proteins comprising a SEQ ID NO:62 fragment need to be tested; only the SEQ ID NO:62 fragments themselves, of which there are a limited number, need be tested.

Second, the Examiner argues the specification provides only a single working example of PfspI. However, as argued in the previous response, U.S. Patent No. 5,795,862 discloses SEQ ID NO:25 and SEQ ID NO:35, both of which have regions of at least 6 (and even 38) contiguous amino acids identical in sequence to at least 6 (or 38) contiguous amino acids from SEQ ID NO:62.

Applicants note they have corrected the priority claim to U.S. Patent No. 5,795,862 and therefore, these sequences are properly considered part of the instant disclosure.

Next, the Examiner contends it is highly unpredictable as to which alterations in a protein sequence would effect the ability of an antibody to bind the altered sequence. Applicants note the claims are to proteins comprising fragments identical in sequence to portions of SEQ ID NO:62; they do not encompass proteins comprising SEQ ID NO:62 fragments that have been altered by substitution or insertion. While the claims do encompass SEQ ID NO:62 sequences altered by addition or deletion, Applicants contend there are a well-defined finite number of such fragments (see paragraph below) and that Applicants have disclosed how to test such fragments for activity.

Finally, the Examiner states undue experimentation would be required to screen all variants of a protein having any function. Applicants disagree. The claims have been drafted so the functional limitation applies to the SEQ ID NO:62 sequence fragment. of at least 6 contiguous amino acids. Therefore, it is only these SEQ ID NO:62 fragments that require testing for the prescribed activity. If one skilled in the art generated every possible 6 contiguous amino acid fragment of SEQ ID NO:62, this only results in 149 fragments that would need to be tested. Even if one generated every possible fragment (from 6 amino acids up to full length), this results in 11,175 possible fragments [n(n+1)/2]. Applicants contend it is certainly possible for one skilled in the art to screen all of these fragments for the prescribed activity using available high-throughput screening methods. While the number of fragments to be screened may seem high, the court in *In re Wands*, 8 USPQ2d, 1400 (CAFC) addressing the issue of undue experimentation stated, "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine...". Similarly, the court in *In re Angstadt*, 190 USPQ 214 (CCPA), noted "The key word is "undue", not "experimentation." Applicants have taught simple assays with which to test such fragments for activity. Furthermore, Applicants contend that such testing, which may constitute a fair amount of work, would be considered routine screening using available high-throughput methods. Based on the arguments presented above, Applicants submit the work required to practice the instant invention does not rise to the level of undue experimentation.

Rejections Under 35 U.S.C. §102(e)

The Examiner has rejected claims 43-45, 57-58 and 61-62 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 5,795,862 and U.S. Patent No. 5,646,115. The Examiner states these patents teach SEQ ID NO:25. Furthermore, U.S. Patent No. 5,796,862 teaches SEQ ID NO:35. According to the Examiner, both sequences comprise at least 38 contiguous amino acids of SEQ ID NO:2.

In response, Applicants note that the instant priority claim has been amended. The instant Application now properly claims priority to both U.S. Patent No. 5,795,862 and v5,646,115. Therefore, neither of these documents can serve as a 102(e) reference.

Double Patenting Rejection

The Examiner has rejected claim 58 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 5,795,862 and claims 58 and 62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 5,646,115. Claim 58 is also provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent Application Serial No. 10/271344.

Applicants note that the appropriate terminal disclaimer(s) will be submitted upon resolution of all other issues discussed herein.

In light of the amendments and remarks above, Applicants request the withdrawal of all rejections and solicit an allowance of the newly submitted claims. The Examiner is invited to contact the undersigned should any issues remain.

Respectfully submitted,

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